In re Application of: Gila MAOR
Serial No.: 10/627,739
Filed: July 28, 2003
Office Action Mailing Date: February 24, 2009

Examiner: Barnhart, Lora Elizabeth
Group Art Unit: 1651
Attorney Docket: 26243

In the claims:

1. (Currently Amended) A method of generating cultured chondrocytes, the method comprising:

(a) isolating chondrocytes from mandibular condyle tissue of a neonatal mammal; and

(b) culturing said isolated chondrocytes, wherein said culturing comprises plating said isolated chondrocytes as a monolayer in the presence of a culturing medium supplemented with serum, ascorbic acid, β glycerol-phosphate, calcium chloride and pyruvate and culturing said isolated chondrocytes for at least 7 days, thereby generating the cultured chondrocytes, wherein the cultured chondrocytes express collagen Type II and not collagen Type I.

2. (Previously Presented) The method of claim 1, wherein step (a) comprises:

(c) selectively removing fibroblast-like cells and/or myocytes from said mandibular condyle tissue, thereby generating modified mandibular condyle tissue depleted of said fibroblast-like cells and/or said myocytes, said modified mandibular condyle tissue including chondrocytes; and

(d) selectively isolating said chondrocytes from said modified mandibular condyle tissue.

3. (Original) The method of claim 2, wherein step (c) is effected by incubating said mandibular condyle tissue with a protease.

4. (Original) The method of claim 2, wherein step (d) is effected by incubating said modified mandibular condyle tissue with a protease so as to selectively release chondrocytes therefrom.

5. (Original) The method of claim 4, further comprising isolating said chondrocytes released from said modified mandibular condyle tissue.

6-10. (Cancelled)

11. (Original) The method of claim 1, wherein step (b) is effected using culturing conditions including a culture medium devoid of at least one supplement selected from the group consisting of a microfilament-modifying compound, a protein kinase inhibitor, and a polypeptide growth factor, wherein said supplement is not derived from a serum supplement of said culture medium.

12. (Withdrawn) The method of claim 11, wherein said microfilament-modifying compound is selected from the group consisting of dihydrocytochalasin B, staurosporine, and an actin filament-modifying compound.

13. (Withdrawn) The method of claim 11, wherein said protein kinase inhibitor is staurosporine and/or a PKC inhibitor.

14. (Original) The method of claim 11, wherein said polypeptide growth factor is selected from the group consisting of TGF, FGF, and IGF.

15. (Withdrawn) The method of claim 14, wherein said TGF is TGF-beta 1.

16. (Withdrawn) The method of claim 14, wherein said FGF is FGF-2.

17. (Original) The method of claim 14, wherein said IGF is IGF-I.

18. (Original) The method of claim 1, wherein step (b) is effected using culturing conditions which are normoxic.

19. (Original) The method of claim 1, wherein step (b) is effected using culturing conditions which include culturing a subconfluent population of said isolated chondrocytes.

20. (Currently Amended) The method of claim 1, wherein step (b) is effected for a minimum duration selected from a range of 14~~5~~-21 days.

21. (Previously Presented) The method of claim 1, wherein step (b) includes passaging said cultured chondrocytes a predetermined number of times.

22. (Previously Presented) The method of claim 21, wherein said predetermined number of times is up to four times.

23. (Cancelled)

24. (Withdrawn) A method of generating cultured endochondral bone cells, the method comprising:

(a) isolating chondrocytes from mandibular condyle tissue; and

(b) culturing said isolated chondrocytes under conditions suitable for formation of endochondral bone cells, thereby generating cultured endochondral bone cells.

25. (Withdrawn) The method of claim 24, wherein step (a) comprises:

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(c) selectively removing fibroblast-like cells and/or myocytes from said mandibular condyle tissue, thereby generating modified mandibular condyle tissue depleted of said fibroblast-like cells and/or said myocytes, said modified mandibular condyle tissue including chondrocytes; and

(d) selectively harvesting said chondrocytes from said modified mandibular condyle tissue.

26. (Withdrawn) The method of claim 25, wherein step (c) is effected by incubating said mandibular condyle tissue with a protease.

27. (Withdrawn) The method of claim 25, wherein step (d) is effected by incubating said modified mandibular condyle tissue with a protease so as to release said chondrocytes therefrom.

28. (Withdrawn) The method of claim 27, further comprising isolating said chondrocytes released from said modified mandibular condyle tissue.

29. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions devoid of a three dimensional support.

30. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions devoid of a biomolecule-coated support.

31. (Withdrawn) The method of claim 29, wherein said three dimensional support is selected from the group consisting of a bead matrix, a gel, a polymer scaffold and a semi-solid substance.

32. (Withdrawn) The method of claim 30, wherein said biomolecule is selected from the group consisting of a polypeptide, an extracellular matrix component, collagen, type I collagen, type II collagen and fibronectin.

33. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions which comprise a culture medium including at least one supplement selected from the group consisting of ascorbic acid, beta-glycerophosphate, pyruvate and IGF-I.

34. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions including a culture medium devoid of at least one supplement selected from the group consisting of a microfilament-modifying compound, a protein kinase inhibitor, and a polypeptide growth factor, wherein said supplement is not derived from a serum supplement of said culture medium.

35. (Withdrawn) The method of claim 34, wherein said microfilament-modifying compound is selected from the group consisting of dihydrocytochalasin B, staurosporine, and an actin filament-modifying compound.

36. (Withdrawn) The method of claim 34, wherein said protein kinase inhibitor is staurosporine and/or a PKC inhibitor.

37. (Withdrawn) The method of claim 34 wherein said polypeptide growth factor is selected from the group consisting of TGF, FGF, and IGF.

38. (Withdrawn) The method of claim 37, wherein said TGF is TGF-beta 1.

39. (Withdrawn) The method of claim 37, wherein said FGF is FGF-2.

40. (Withdrawn) The method of claim 37, wherein said IGF is IGF-I.

41. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions which are normoxic.

42. (Withdrawn) The method of claim 24, wherein step (b) is effected using culturing conditions which include culturing a subconfluent population of said isolated chondrocytes.

43. (Withdrawn) The method of claim 24, wherein step (b) is effected for a minimum duration selected from a range of 14-21 days.

44. (Withdrawn) The method of claim 24, wherein said mandibular condyle tissue is derived from a mammal.

45. (Withdrawn) A method of redifferentiating dedifferentiated chondrocytes, the method comprising culturing dedifferentiated chondrocytes under culturing conditions which comprise a culture medium including at least one supplement selected from the group consisting of ascorbic acid, beta-glycerophosphate, pyruvate and IGF-I, said culturing conditions being devoid of a three dimensional support and/or of a biomolecule-coated support, thereby redifferentiating said dedifferentiated chondrocytes.

46. (Withdrawn) The method of claim 45, wherein said culture medium is devoid of at least one supplement selected from the group consisting of a microfilament-modifying compound, a protein kinase inhibitor, and a polypeptide growth factor, wherein said supplement selected from the group consisting of a

microfilament-modifying compound, a protein kinase inhibitor, and a polypeptide growth factor is not derived from a serum supplement of said culture medium.

47. (Withdrawn) The method of claim 46, wherein said microfilament-modifying compound is selected from the group consisting of dihydrocytochalasin B, staurosporine, and an actin filament-modifying compound.

48. (Withdrawn) The method of claim 46, wherein said protein kinase inhibitor is staurosporine and/or a PKC inhibitor.

49. (Withdrawn) The method of claim 46, wherein said polypeptide growth factor is selected from the group consisting of TGF, FGF, and IGF.

50. (Withdrawn) The method of claim 49, wherein said TGF is TGF-beta 1.

51. (Withdrawn) The method of claim 49, wherein said FGF is FGF-2.

52. (Withdrawn) The method of claim 49, wherein said IGF is IGF-I.

53. (Withdrawn) The method of claim 45, wherein said three dimensional support is selected from the group consisting of a bead matrix, a gel, a polymer scaffold and a semi-solid substance.

54. (Withdrawn) The method of claim 45, wherein said biomolecule is selected from the group consisting of a polypeptide, an extracellular matrix component, collagen, type I collagen, type II collagen and fibronectin.

55. (Withdrawn) The method of claim 45, wherein said culturing conditions are normoxic.

56. (Withdrawn) The method of claim 45, wherein said culturing conditions further comprise culturing a subconfluent population of said dedifferentiated chondrocytes.

57. (Withdrawn) The method of claim 45, wherein culturing is effected for a minimum duration selected from a range of 1-6 days.

58. (Withdrawn) The method of claim 45, wherein said dedifferentiated chondrocytes are derived from mandibular condyle tissue.

59. (Withdrawn) The method of claim 58, wherein said mandibular condyle tissue is derived from a subadult organism and/or from a mouse.

60. (Withdrawn) Isolated mandibular condyle tissue comprising chondrocytes and being depleted of fibroblast-like cells and/or myocytes.

61. (Withdrawn) The isolated mandibular condyle tissue of claim 60, wherein said mandibular condyle tissue is mostly or completely depleted of fibroblast-like cells and/or myocytes.

62. (Withdrawn) The isolated mandibular condyle tissue of claim 60, wherein said mandibular condyle tissue is derived from a mammal.

63. (Withdrawn) A cell culture comprising isolated chondrocytes being capable of generating endochondral bone cells when cultured under culturing conditions which:

(i) include a two dimensional support not coated with a biomolecule; and

(ii) a culture medium devoid of a supplement selected from the group consisting of a microfilament-modifying compound, a protein kinase inhibitor and a polypeptide growth factor, said supplement not being derived from a serum supplement of said culture medium.

64. (Withdrawn) The cell culture of claim 63, wherein said culturing conditions are devoid of a three dimensional support.

65. (Withdrawn) The cell culture of claim 63, wherein said culturing conditions are devoid of a biomolecule-coated support.

66. (Withdrawn) The cell culture of claim 64, wherein said three dimensional support is selected from the group consisting of a bead matrix, a gel, a polymer scaffold and a semi-solid substance.

67. (Withdrawn) The cell culture of claim 65, wherein said biomolecule is selected from the group consisting of a polypeptide, an extracellular matrix component, collagen, type I collagen, type II collagen and fibronectin.

68. (Withdrawn) The cell culture of claim 63, wherein said culture medium includes at least one supplement selected from the group consisting of ascorbic acid, beta-glycerophosphate, pyruvate and IGF-I.

69. (Withdrawn) The cell culture of claim 63, wherein said microfilament-modifying compound is selected from the group consisting of dihydrocytochalasin B, staurosporine, and an actin filament-modifying compound.

70. (Withdrawn) The cell culture of claim 63, wherein said protein kinase inhibitor is staurosporine and/or a PKC inhibitor.

71. (Withdrawn) The cell culture of claim 63, wherein said polypeptide growth factor is selected from the group consisting of TGF, FGF, and IGF.

72. (Withdrawn) The cell culture of claim 71, wherein said TGF is TGF-beta 1.

73. (Withdrawn) The cell culture of claim 71, wherein said FGF is FGF-2.

74. (Withdrawn) The cell culture of claim 71, wherein said IGF is IGF-I.

75. (Withdrawn) The cell culture of claim 63, wherein said culturing conditions are normoxic.

76. (Withdrawn) The cell culture of claim 63, wherein said culturing conditions include culturing a subconfluent population of said isolated chondrocytes.

77. (Withdrawn) The cell culture of claim 63, wherein said isolated chondrocytes are capable of generating said endochondral bone cells when cultured for a minimum duration selected from a range of 14-21 days.

78. (Withdrawn) The cell culture of claim 63, wherein said isolated chondrocytes are derived from mandibular condyle tissue.

79. (Withdrawn) The cell culture of claim 78, wherein said mandibular condyle tissue is derived from a mammal.

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80. (Withdrawn) A method of treating a cartilage or bone disease in a subject, the method comprising:

(a) isolating chondrocytes from mandibular condyle tissue;

(b) culturing said isolated chondrocytes, thereby generating cultured chondrocytes; and

(c) administering a therapeutically effective dose of said cultured chondrocytes to the subject, thereby treating the cartilage or bone disease in the subject.

81. (Withdrawn) The method of claim 80, further comprising isolating said cultured chondrocytes prior to step (c).

82. (Withdrawn) The method of claim 80, wherein step (a) comprises:

(d) selectively removing fibroblast-like cells and/or myocytes from said mandibular condyle tissue, thereby generating modified mandibular condyle tissue depleted of said fibroblast-like cells and/or said myocytes, said modified mandibular condyle tissue including chondrocytes; and

(e) selectively harvesting said chondrocytes from said modified mandibular condyle tissue.

83. (Withdrawn) The method of claim 82, wherein step (d) is effected by incubating said mandibular condyle tissue with a protease.

84. (Withdrawn) The method of claim 82, wherein step (e) is effected by incubating said modified mandibular condyle tissue with a protease so as to selectively release chondrocytes therefrom.

85. (Withdrawn) The method of claim 84, further comprising isolating said chondrocytes released from said modified mandibular condyle tissue.

86. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions devoid of a three dimensional support.

87. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions devoid of a biomolecule-coated support.

88. (Withdrawn) The method of claim 86, wherein said three dimensional support is selected from the group consisting of a bead matrix, a gel, a polymer scaffold and a semi-solid substance.

89. (Withdrawn) The method of claim 87, wherein said biomolecule is selected from the group consisting of a polypeptide, an extracellular matrix component, collagen, type I collagen, type II collagen and fibronectin.

90. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions which comprise a culture medium including at least one supplement selected from the group consisting of ascorbic acid, beta-glycerophosphate, pyruvate and IGF-I.

91. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions including a culture medium devoid of at least one supplement selected from the group consisting of a microfilament-modifying compound, a protein kinase inhibitor, and a polypeptide growth factor, wherein said supplement is not derived from a serum supplement of said culture medium.

92. (Withdrawn) The method of claim 91, wherein said microfilament-modifying compound is selected from the group consisting of dihydrocytochalasin B, staurosporine, and an actin filament-modifying compound.

93. (Withdrawn) The method of claim 91, wherein said protein kinase inhibitor is staurosporine and/or a PKC inhibitor.

94. (Withdrawn) The method of claim 91, wherein said polypeptide growth factor is selected from the group consisting of TGF, FGF, and IGF.

95. (Withdrawn) The cell culture of claim 94, wherein said TGF is TGF-beta 1.

96. (Withdrawn) The cell culture of claim 94, wherein said FGF is FGF-2.

97. (Withdrawn) The cell culture of claim 94, wherein said IGF is IGF-I.

98. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions which are normoxic.

99. (Withdrawn) The method of claim 80, wherein step (b) is effected using culturing conditions which include culturing a subconfluent population of said isolated chondrocytes.

100. (Withdrawn) The method of claim 80, wherein step (b) is effected for a minimum duration selected from a range of 5-21 days.

101. (Withdrawn) The method of claim 80, wherein step (b) includes passaging said cultured chondrocytes a predetermined minimum number of times.

102. (Withdrawn) The method of claim 101, wherein said predetermined minimum number of times is four times.

103. (Withdrawn) The method of claim 80, wherein said mandibular condyle tissue is derived from a mammal.

104. – 107. (Cancelled)

108. (Previously Presented) The method of claim 1, wherein the cultured chondrocytes are cultured primary chondrocytes.